1: Oral Surg Oral Med Oral Pathol 1990 Jan;69(1):42-4

Combination immunosuppressant and topical steroid therapy for treatment of recurrent major aphthae. A case report.

Brown RS, Bottomley WK.

Department of Oral Diagnostic Sciences, University of Texas Health Science Center, Houston.

A 32-year-old woman with a 3-month history of severe major aphthous stomatitis covering the anterior dorsal third of the tongue was treated successfully with topical dexamethasone mouthrinse and oral azathioprine tablets. The lesion was resolved within 90 days without side effects.

PMID: 2296449 [PubMed - indexed for MEDLINE]

1: Br J Oral Surg 1972 Mar;9(3):233-6

Treatment of aphthous ulceration with topical azathioprine. A double blind trial.

Eggleston DJ, Nally FF.

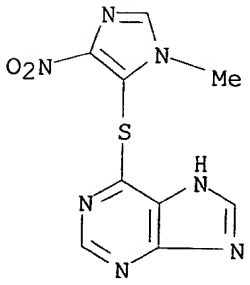
Publication Types:
- Clinical Trial
- Randomized Controlled Trial

PMID: 4558236 [PubMed - indexed for MEDLINE]

L2 1 AZATHIOPRINE/CN

=> d

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 446-86-6 REGISTRY
CN 1H-Purine, 6-[(1-methyl-4-nitro-1H-imidazol-5-yl)thio]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Purine, 6-[(1-methyl-4-nitroimidazol-5-yl)thio]- (6CI, 8CI)
OTHER NAMES:
CN 6-(1-Methyl-4-nitroimidazol-5-yl)thiopurine
CN 6-(1-Methyl-4-nitromidazol-5-ylthio)purine
CN Azamune
CN Azanin
CN Azathioprin
CN **Azathioprine**
CN Azoran
CN Azothioprine
CN BW 57-322
CN Imuran
CN Imurek
CN Imurel
CN Muran
CN NSC 39084
FS 3D CONCORD
DR 11120-16-4, 6165-04-4, 33609-91-5
MF C9 H7 N7 O2 S
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS*, SYNTHLINE, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1920 REFERENCES IN FILE CA (1967 TO DATE)
20 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1926 REFERENCES IN FILE CAPLUS (1967 TO DATE)
27 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

```
=> fil caplus uspatfull medline
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                          ENTRY     SESSION
FULL ESTIMATED COST                                        9.96       10.17

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FILE 'USPATFULL' ENTERED AT 17:20:29 ON 17 MAY 2002
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FILE 'MEDLINE' ENTERED AT 17:20:29 ON 17 MAY 2002

=> s azathioprine or  446-86-6/rn
'RN' IS NOT A VALID FIELD CODE
L3        16484 AZATHIOPRINE OR 446-86-6/RN

=> s aphtae or lichen or pemphigoid or pemphigus
L4        22596 APHTAE OR LICHEN OR PEMPHIGOID OR PEMPHIGUS

=> s l3 and l4
L5          439 L3 AND L4

=> s mouth
L6       184794 MOUTH

=> s l5 and l6
L7           71 L5 AND L6

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8           71 DUP REM L7 (0 DUPLICATES REMOVED)

=> s l8 and py<1999
L9           18 L8 AND PY<1999

=> d l9

L9   ANSWER 1 OF 18  USPATFULL
AN      1998:150961  USPATFULL
TI      Methods and bicyclic polyamine compositions for the treatment of
        inflammation
IN      Bergeron, Jr., Raymond J., Gainesville, FL, United States
PA      University of Florida Research Foundation, Inc., Gainesville, FL,
United
        States (U.S. corporation)
PI      US 5843959               19981201                                <--
AI      US 1997-820027           19970319 (8)
DT      Utility
FS      Granted
LN.CNT 1074
INCL    INCLM: 514/316.000
        INCLS: 514/183.000; 514/212.000; 514/326.000; 514/422.000
NCL     NCLM:  514/316.000
        NCLS:  514/183.000; 514/217.030; 514/217.040; 514/217.080; 514/326.000;
               514/422.000
```

IC [6]
ICM: A61K031-445
ICS: A61K031-33; A61K031-55; A61K031-40
EXF 514/316; 514/326; 514/212; 514/183; 514/422
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d ab

L9 ANSWER 1 OF 18 USPATFULL
AB Methods for treating inflammatory conditions wherein the active agent is

a polyamine having the formula set forth below: ##STR1## or a salt thereof with a pharmaceutically acceptable acid wherein: R.sub.1, R.sub.2, R.sub.3 and R.sub.4 may be the same or different and represent H, straight- or branched-chain alkyl, aryl, aryl alkyl or cycloalkyl of 1-12 carbon atoms;

a, b, c and d may be the same or different and are integers from 0 to 8,

except that when a or c is zero, b or d is greater than or equal to 3 and when a or c is one, b or d is greater than or equal to 2; and

X, Y and Z may be the same or different; X and Z are integers from 0 to 10; and Y is an integer from 1 to 10, excluding the polyamine of the formula wherein a=b=c=d=2, X=Z=2 and Y=4.

=> d kwic

L9 ANSWER 1 OF 18 USPATFULL
PI US 5843959 19981201 <--
SUMM . . . as aurothiomalate; anti-rheumatic agents such as chloroquine preparations and D-penicillamine; anti-gout agents such as colchicine; and immuno-suppressors such as cyclophosphamide, **azathioprine**, methotrexate and levamisole.
DETD . . . in treating inflammatory and hyperproliferative skin diseases such as psoriasis, atopical dermatitis, contact dermatitis and further eczematous dermatitises, seborrhoeic dermatitis, **Lichen** planus, **Pemphigus**, bullous **Pemphigoid**, Epidermolysis bullosa, urticaria, angioedemas, vasculitides, erythemas, cutaneous eosinophilias, Lupus erythematosus and acne, and in situations of organ or tissue transplantation. . .
DETD . . . of the present invention resides in the fact that the bicyclic polyamine are orally active. Oral availability allows administration by **mouth** and renders the present invention particularly suitable for use in treating conditions involving chronic inflammation such as arthritis.

=> d 2-19

L9 ANSWER 2 OF 18 USPATFULL
AN 1998:88829 USPATFULL
TI Camptothecin drug combinations and methods with reduced side effects
IN Ratain, Mark J., Chicago, IL, United States
Gupta, Elora, Chicago, IL, United States
PA Arch Development Corporation, Chicago, IL, United States (U.S. corporation)
PI US 5786344 19980728 <--

AI US 1995-423641 19950417 (8)
RLI Continuation-in-part of Ser. No. US 1994-271278, filed on 5 Jul 1994, now abandoned
DT Utility
FS Granted
LN.CNT 4037
INCL INCLM: 514/100.000
INCLS: 514/211.000
NCL NCLM: 514/100.000
NCLS: 424/143.100; 514/009.000; 514/028.000; 514/171.000; 514/183.000; 514/211.070; 514/211.080
IC [6]
ICM: A61K031-545
ICS: A61K031-47
EXF 514/100; 514/211
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 3 OF 18 USPATFULL
AN 1998:33937 USPATFULL
TI Use of **azathioprine** to treat crohn's disease
IN Sandborn, William J., Rochester, MN, United States
PA Glaxo Wellcome Inc., Research Triangle Park, NC, United States (U.S. corporation)
PI US 5733915 19980331 <--
AI US 1995-413783 19950330 (8)
DT Utility
FS Granted
LN.CNT 662
INCL INCLM: 514/262.000
INCLS: 514/391.000; 514/395.000
NCL NCLM: 514/263.300
NCLS: 514/391.000; 514/395.000
IC [6]
ICM: A61K031-52
ICS: A61K031-415
EXF 514/391; 514/395; 514/262
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 4 OF 18 USPATFULL
AN 97:68480 USPATFULL
TI Treatment of inflammatory and/or autoimmune dermatoses with thalidomide alone or in combination with other agents
IN Andrulis, Jr., Peter J., Bethesda, MD, United States
Drulak, Murray W., Gaithersburg, MD, United States
PA Andrulis Pharmaceuticals, Beltsville, MD, United States (U.S. corporation)
PI US 5654312 19970805 <--
AI US 1995-475426 19950607 (8)
DT Utility
FS Granted
LN.CNT 925
INCL INCLM: 514/279.000
INCLS: 514/290.000; 514/291.000; 514/292.000; 514/323.000; 514/408.000; 514/410.000; 514/411.000; 514/422.000; 514/424.000; 514/425.000; 424/450.000
NCL NCLM: 514/279.000
NCLS: 424/450.000; 514/290.000; 514/291.000; 514/292.000; 514/323.000; 514/408.000; 514/410.000; 514/411.000; 514/422.000; 514/424.000; 514/425.000
IC [6]

ICM: A61K031-445
EXF 514/279; 514/290; 514/291; 514/292; 514/323; 514/408; 514/410; 514/411; 514/422; 514/424; 514/425; 424/450
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 5 OF 18 USPATFULL
AN 97:49665 USPATFULL
TI Method for treating diseases mediated by proteases
IN Sharpe, Richard J., Gloucester, MA, United States
McAloon, Maureen H., Boston, MA, United States
Galli, Stephen J., Winchester, MA, United States
Arndt, Kenneth A., Newton Centre, MA, United States
PA Arcturus Pharmaceutical Corporation, Woburn, MA, United States (U.S. corporation)
PI US 5637616 19970610 <--
AI US 1993-131892 19931005 (8)
RLI Continuation-in-part of Ser. No. US 1993-79645, filed on 18 Jun 1993, now abandoned
DT Utility
FS Granted
LN.CNT 1049
INCL INCLM: 514/562.000
INCLS: 514/028.000; 514/029.000; 514/030.000; 514/251.000; 514/291.000; 514/457.000; 514/513.000; 514/538.000; 514/549.000; 514/552.000; 514/554.000; 514/555.000; 554/085.000; 554/101.000; 554/102.000; 558/230.000; 558/256.000; 558/257.000; 560/016.000; 560/147.000; 560/153.000; 562/426.000; 562/557.000
NCL NCLM: 514/562.000
NCLS: 514/028.000; 514/029.000; 514/030.000; 514/251.000; 514/291.000; 514/457.000; 514/513.000; 514/538.000; 514/549.000; 514/552.000; 514/554.000; 514/555.000; 554/085.000; 554/101.000; 554/102.000; 558/230.000; 558/256.000; 558/257.000; 560/016.000; 560/147.000; 560/153.000; 562/426.000; 562/557.000
IC [6]
ICM: C07C323-59
ICS: A61K031-195; A61K031-20
EXF 562/556; 562/426; 562/557; 514/562; 514/28; 514/29; 514/30; 514/251; 514/291; 514/457; 514/513; 514/538; 514/549; 514/552; 514/554; 514/555; 554/85; 554/101; 554/102; 558/230; 558/256; 558/257; 560/16; 560/147; 560/153
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 6 OF 18 USPATFULL
AN 93:76520 USPATFULL
TI Topical application of spiperone or derivatives thereof for treatment of
pathological conditions associated with immune responses
IN Sharpe, Richard J., Gloucester, MA, United States
Arndt, Kenneth A., Newton Centre, MA, United States
Galli, Stephen J., Winchester, MA, United States
PA Beth Israel Hospital Association, Boston, MA, United States (U.S. corporation)
PI US 5244902 19930914 <--
AI US 1992-831429 19920205 (7)
RLI Continuation-in-part of Ser. No. US 1990-494744, filed on 16 Mar 1990, now abandoned which is a continuation-in-part of Ser. No. US 1989-396523, filed on 21 Aug 1989, now abandoned
DT Utility
FS Granted
LN.CNT 931

INCL INCLM: 514/278.000
INCLS: 514/885.000
NCL NCLM: 514/278.000
NCLS: 514/885.000
IC [5]
ICM: A61K031-44
EXF 514/278; 514/885
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 7 OF 18 USPATFULL
AN 93:16468 USPATFULL
TI Methods for the treatment of demyelinating disease, uveitis, or graft-versus-host disease using TNF
IN Otsuka, Yoshiki, Fuji, Japan
Hori, Kazuyoshi, Fuji, Japan
Hayashi, Hiroshi, Fuji, Japan
PA Asahi Kasei Kogyo Kabushiki Kaisha, Osaka, Japan (non-U.S. corporation)
PI US 5190750 19930302 <--
AI US 1991-665876 19910307 (7)
PRAI JP 1990-56734 19900309
JP 1990-56735 19900309
JP 1990-56736 19900309
DT Utility
FS Granted
LN.CNT 513
INCL INCLM: 424/085.100
INCLS: 514/012.000; 514/021.000
NCL NCLM: 424/085.100
NCLS: 514/012.000; 514/021.000
IC [5]
ICM: A61K037-02
EXF 514/12; 514/21; 424/85.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 8 OF 18 MEDLINE
AN 96288160 MEDLINE
DN 96288160 PubMed ID: 8689773
TI Erosive and generalized **lichen** planus responsive to **azathioprine**.
AU Lear J T; English J S
CS Department of Dermatology, North Staffs NHS Trust, Stoke on Trent, UK.
SO CLINICAL AND EXPERIMENTAL DERMATOLOGY, **(1996 Jan)** 21 (1) 56-7.
Journal code: DDU; 7606847. ISSN: 0307-6938.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199608
ED Entered STN: 19960911
Last Updated on STN: 19960911
Entered Medline: 19960826

L9 ANSWER 9 OF 18 MEDLINE
AN 93260146 MEDLINE
DN 93260146 PubMed ID: 8491885
TI **Pemphigus** vulgaris and pregnancy: risk factors and recommendations.
AU Goldberg N S; DeFeo C; Kirshenbaum N
CS Department of Dermatology, New York Medical College.
SO JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY, **(1993 May)** 28 (5

Pt 2) 877-9.
Journal code: HVG; 7907132. ISSN: 0190-9622.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199306
ED Entered STN: 19930625
Last Updated on STN: 19930625
Entered Medline: 19930615

L9 ANSWER 10 OF 18 MEDLINE
AN 93219869 MEDLINE
DN 93219869 PubMed ID: 8465228
TI Cicatricial **pemphigoid**.
AU Warren S D; Lesher J L Jr
CS Department of Dermatology, Medical College of Georgia, Augusta 30912-2900.
SO SOUTHERN MEDICAL JOURNAL, **(1993 Apr)** 86 (4) 461-4.
Journal code: UVH; 0404522. ISSN: 0038-4348.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199305
ED Entered STN: 19930521
Last Updated on STN: 19930521
Entered Medline: 19930506

L9 ANSWER 11 OF 18 MEDLINE
AN 92375486 MEDLINE
DN 92375486 PubMed ID: 1508510
TI Oral presentation of **pemphigus** vulgaris and its response to systemic steroid therapy.
AU Lamey P J; Rees T D; Binnie W H; Wright J M; Rankin K V; Simpson N B
CS Department of Oral Medicine and Pathology, Glasgow Dental Hospital and School, Scottland.
SO ORAL SURGERY, ORAL MEDICINE, AND ORAL PATHOLOGY, **(1992 Jul)** 74 (1) 54-7.
Journal code: OJU; 0376406. ISSN: 0030-4220.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Dental Journals; Priority Journals
EM 199209
ED Entered STN: 19921009
Last Updated on STN: 19921009
Entered Medline: 19920918

L9 ANSWER 12 OF 18 MEDLINE
AN 92375485 MEDLINE
DN 92375485 PubMed ID: 1508509
TI Mucous membrane **pemphigoid**. Treatment experience at two institutions.
AU Lamey P J; Rees T D; Binnie W H; Rankin K V
CS Department of Oral Medicine, Glasgow Dental Hospital and School, Scotland.
SO ORAL SURGERY, ORAL MEDICINE, AND ORAL PATHOLOGY, **(1992 Jul)** 74 (1) 50-3.
Journal code: OJU; 0376406. ISSN: 0030-4220.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Dental Journals; Priority Journals
EM 199209
ED Entered STN: 19921009
Last Updated on STN: 19921009
Entered Medline: 19920918

L9 ANSWER 13 OF 18 MEDLINE
AN 92253187 MEDLINE
DN 92253187 PubMed ID: 1812447
TI A prospective study of findings and management in 214 patients with oral **lichen** planus.
AU Silverman S Jr; Gorsky M; Lozada-Nur F; Giannotti K
CS School of Dentistry, University of California, San Francisco 94143.
SO ORAL SURGERY, ORAL MEDICINE, AND ORAL PATHOLOGY, **(1991 Dec)** 72 (6) 665-70.
Journal code: OJU; 0376406. ISSN: 0030-4220.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Dental Journals; Priority Journals
EM 199206
ED Entered STN: 19920619
Last Updated on STN: 19920619
Entered Medline: 19920608

L9 ANSWER 14 OF 18 MEDLINE
AN 91297019 MEDLINE
DN 91297019 PubMed ID: 2068258
TI **Pemphigus** vulgaris of the oral mucosa: report of two cases.
AU Raghoebar G M; Brouwer T J; Schoots C J
CS University Hospital Groningen, The Netherlands.
SO QUINTESSENCE INTERNATIONAL, **(1991 Mar)** 22 (3) 199-202.
Journal code: QLP; 0342677. ISSN: 0033-6572.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Dental Journals
EM 199108
ED Entered STN: 19910901
Last Updated on STN: 19910901
Entered Medline: 19910815

L9 ANSWER 15 OF 18 MEDLINE
AN 91293931 MEDLINE
DN 91293931 PubMed ID: 2066193
TI Oral **pemphigus** vulgaris in young adults.
AU Firth N; Rich A; Varigos G; Reade P C
CS Section of Oral Medicine and Oral Surgery, School of Dental Science, University of Melbourne, Victoria, Australia.
SO INTERNATIONAL JOURNAL OF DERMATOLOGY, **(1991 May)** 30 (5) 352-6.
Journal code: GR2; 0243704. ISSN: 0011-9059.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199108
ED Entered STN: 19910901

Last Updated on STN: 19910901
Entered Medline: 19910812

L9 ANSWER 16 OF 18 MEDLINE
AN 91009989 MEDLINE
DN 91009989 PubMed ID: 2212117
TI Photochemotherapy improves chronic cutaneous graft-versus-host disease.
AU Volc-Platzer B; Honigsmann H; Hinterberger W; Wolff K
CS Department of Dermatology I, University of Vienna, Austria.
SO JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY, **(1990 Aug)** 23 (2 Pt 1) 220-8.
Journal code: HVG; 7907132. ISSN: 0190-9622.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199011
ED Entered STN: 19910117
Last Updated on STN: 19910117
Entered Medline: 19901115

L9 ANSWER 17 OF 18 MEDLINE
AN 90188943 MEDLINE
DN 90188943 PubMed ID: 2179535
TI Vesiculo-bullous mucocutaneous disease: benign mucous membrane and bullous **pemphigoid**.
AU Williams D M
CS Department of Oral Pathology, London Hospital Medical College, England.
SO JOURNAL OF ORAL PATHOLOGY AND MEDICINE, **(1990 Jan)** 19 (1) 16-23.
Ref: 94
Journal code: JRF; 8911934. ISSN: 0904-2512.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Dental Journals; Priority Journals
EM 199004
ED Entered STN: 19900601
Last Updated on STN: 19900601
Entered Medline: 19900419

L9 ANSWER 18 OF 18 MEDLINE
AN 74131794 MEDLINE
DN 74131794 PubMed ID: 4819136
TI **Azathioprine** in the treatment of muco-cutaneous **pemphigoid**.
AU Dave V K; Vickers C F
SO BRITISH JOURNAL OF DERMATOLOGY, **(1974 Feb)** 90 (2) 183-6.
Journal code: AW0; 0004041. ISSN: 0007-0963.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197405
ED Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19740529

=> d 19 18 ab

L9 ANSWER 18 OF 18 MEDLINE

=> d 19 15 ab

L9 ANSWER 15 OF 18 MEDLINE
AB Three patients, aged 31, 26, and 22 years, had **pemphigus** vulgaris. A delay in diagnosis and appropriate treatment occurred because the initial presentation was confined to the oral mucosa.

=> d 19 15 kwic

L9 ANSWER 15 OF 18 MEDLINE
TI Oral **pemphigus** vulgaris in young adults.
SO INTERNATIONAL JOURNAL OF DERMATOLOGY, **(1991 May)** 30 (5) 352-6.
Journal code: GR2; 0243704. ISSN: 0011-9059.
AB Three patients, aged 31, 26, and 22 years, had **pemphigus** vulgaris. A delay in diagnosis and appropriate treatment occurred because the initial presentation was confined to the oral mucosa.
CT Check Tags: Case Report; Female; Human; Male
Adult
*Autoimmune Diseases: DT, drug therapy
Autoimmune Diseases: PA, pathology
Azathioprine: TU, therapeutic use
Candidiasis, Oral: CO, complications
Candidiasis, Oral: DT, drug therapy
***Mouth Diseases: DT, drug therapy**
Mouth Diseases: PA, pathology
***Pemphigus: DT, drug therapy**
Pemphigus: PA, pathology
Prednisolone: TU, therapeutic use
RN **446-86-6 (Azathioprine)**; 50-24-8 (Prednisolone)

=> d 19 14 ab kwic

L9 ANSWER 14 OF 18 MEDLINE
AB Two cases of **pemphigus** vulgaris in which oral lesions were the first signs of the disease are reported. The clinical signs and symptoms, histologic characteristics, and immunohistochemistry are discussed. Early recognition of oral lesions associated with the disease is of the utmost prognostic value. Treatment, which can only be symptomatic, usually consists of a combination of a corticosteroid and immunosuppressive medication. Because side effects may be serious, these medications should be prescribed and monitored by an experienced dermatologist.
TI **Pemphigus** vulgaris of the oral mucosa: report of two cases.
SO QUINTESSENCE INTERNATIONAL, **(1991 Mar)** 22 (3) 199-202.
Journal code: QLP; 0342677. ISSN: 0033-6572.
AB Two cases of **pemphigus** vulgaris in which oral lesions were the first signs of the disease are reported. The clinical signs and symptoms, histologic. . .
CT Check Tags: Case Report; Female; Human
Adrenal Cortex Hormones: TU, therapeutic use
Adult
Age Factors
Azathioprine: TU, therapeutic use

Mouth Diseases: DT, drug therapy
Mouth Diseases: PA, pathology
***Mouth Mucosa: PA, pathology**
Pemphigus: DT, drug therapy
***Pemphigus: PA, pathology**
RN **446-86-6 (Azathioprine)**

=> d 2-13 ab kwic

L9 ANSWER 2 OF 18 USPATFULL
AB This invention provides methods and combination formulations and kits to reduce the toxicity of camptothecin drugs, such as irinotecan (CPT-11). Disclosed are therapeutics and treatment methods employing such drugs in combination with agents that increase conjugative enzyme activity or glucuronosyltransferase activity, and agents that decrease biliary transport protein activity, such as cyclosporine A, the resultant effects of which are to decrease the significant side effects previously associated with treatment using these drugs.
PI US 5786344 19980728 <--
DETD . . . tablet daily, preferably at bedtime, for 7 to 14 consecutive days; 10 mg as a troche, slowly dissolved in the **mouth** 5 times a day. It is available in dosage forms of cream: 1%; vaginal cream: 1% (one applicator full contains. . .
DETD . . . aplastic anemia, some cases of myasthenia gravis, childhood diabetes (Type I) of recent onset, Graves' disease, Crohn's disease, multiple sclerosis, **pemphigus** and **pemphigoid**, dermatomyositis, polymyositis, atopic dermatitis, severe psoriasis, Bechcet's disease, uveitis, biliary cirrhosis and pulmonary sarcoidosis.
It usually is employed in combination. . .
DETD Lennard et al., "Pharmacogenetics of acute **azathioprine** toxicity:

L9 ANSWER 3 OF 18 USPATFULL
AB A therapeutic method for the treatment of Crohn's disease is provided, comprising administering to a patient in need of said treatment an intravenous dose of **azathioprine** or a pharmaceutically acceptable derivative thereof.
TI Use of **azathioprine** to treat crohn's disease
PI US 5733915 19980331 <--
AB . . . treatment of Crohn's disease is provided, comprising administering to a patient in need of said treatment an intravenous dose of **azathioprine** or a pharmaceutically acceptable derivative thereof.
SUMM . . . which is refractory to standard medical therapy and fistulous Crohn's disease which is refractory to metronidazole are often treated with **azathioprine** (AZA) or its metabolite 6-mercaptopurine (6-MP).
SUMM . . . need of immunosuppression, such as a patient afflicted with Crohn's disease or another immunoregulatory disorder, a continuous intravenous infusion of **azathioprine** (AZA), 6-MP, or a pharmaceutically acceptable salt thereof, at a dosing rate effective to substantially accelerate the onset of the immunosuppressive action of **azathioprine**, 6-MP, or a pharmaceutically acceptable salt thereof, in said patient. A dose of about 1500-5900 mg of

azathioprine is administered to an adult patient over a period of about 30-40 hours via a continuous intravenous infusion. This is. . . rate of about 35-200 mg/hour. For example, in the working example presented hereinbelow, the dosing rate for intravenous administration of

azathioprine is 50 mg/hr for a total of 1800 mg over 36 hours. The **azathioprine**, 6-MP, or a pharmaceutically acceptable salt thereof, is preferably administered in combination with a pharmaceutically acceptable liquid carrier.

SUMM A preferred embodiment of the invention comprises the intravenous administration of **azathioprine** followed by oral administration of **azathioprine** at 1-2.5 mg/kg/day, for at least 16 weeks, up to periods of time of about 1-2 years. 6-Thioguanine nucleotide concentrations. . . of about 50-500 pmol/10.sup.8 red blood cells for

at least 4 months after intravenous therapy, while the patient is taking

azathioprine orally. The 6-methylmercaptopurine concentration in red blood cells is preferably about 1000-7000 pmol/10.sup.8 red blood cells after intravenous therapy is. . .

SUMM For example, a human patient to be treated with **azathioprine**, 6-MP, or a pharmaceutically acceptable salt thereof, may be afflicted with active inflammatory Crohn's disease, Crohn's fistulous disease, or steroid. . . refractory to standard medical therapy. Patients can be selected who exhibit a Crohn's Disease Activity Index (CDAI) before continuous intravenous **azathioprine** therapy of about 250, or more. As used herein, the term "substantially accelerate" is defined as reducing a patient's CDAI by at least 100 points in less than about one month following the completion of continuous intravenous **azathioprine** therapy. The CDAI score can be decreased by a reduction in either or both the number or severity of symptoms, based on

objective or subjective criteria, as discussed hereinbelow. In contrast,

the oral administration of **azathioprine** at 1-2.5 mg/kg/day for about three to four months is required to achieve a similarly significant therapeutic effect. Thus, oral. . .

DETD . . . goal of treatment is to obtain a dosing rate effective to substantially accelerate the onset of the immunosuppressive action of **azathioprine** in said patient, over that achievable by conventional oral dosing of AZA, i.e., 1-2.5 mg/kg/day.

DETD . . . Total number of the following symptoms

or findings present during the week:

(1) arthritis or arthralgia

(2) skin or **mouth** lesions (e.g., pyoderma gangrenosum, erythema nodosum, aphthous stomatitis)

(3) iritis or uveitis

(4) anal fissure, fistula, or perirectal abscess

(5). . .

DETD . . . or after solid organ transplantation, or in the treatment of other autoimmune disorders, including rheumatoid arthritis, ulcerative colitis, psoriasis, bullous **pemphigoid**, eczema, dermatomyocytis, polymyositis, Wegener's granulomatosis, pyoderma grangenosum, idiopathic thrombocytopenia purpura, and Behcet's syndrome.

CLM What is claimed is:

. . . disease comprising administering to a human patient afflicted with Crohn's disease that is corticosteroid intolerant a continuous

intravenous infusion of **azathioprine**, 6-MP, or a pharmaceutically acceptable salt thereof, at a dosing rate and for a period effective to substantially accelerate the onset of the immunosuppressive action of **azathioprine** over the time required for said onset when **azathioprine** is administered orally.

2. The method of claim 1 wherein an effective amount of **azathioprine**, 6-MP, or a pharmaceutically acceptable salt thereof, is administered in combination with a pharmaceutically acceptable liquid carrier.

3. The method of claim 1 wherein **azathioprine** is administered intravenously at about 35-200 mg/hour.

4. The method of claim 1 wherein the intravenous infusion of **azathioprine** delivers about 1500-5900 mg over a period of about 30-40 hours.

7. The method of claim 1 further comprising administering **azathioprine** orally following intravenous administration.

. . . is afflicted with active inflammatory Crohn's disease and the Crohn's
Disease Activity Index (CDAI) score of that patient before intravenous **azathioprine** therapy is .gtoreq.250.

IT **446-86-6**, Azathioprine
(i.v. infusion of azathioprine or 6-mercaptopurine for Crohn's disease treatment)

L9 ANSWER 4 OF 18 USPATFULL
AB Methods of treatment for inflammatory and autoimmune dermatoses which comprises topical and/or systemic administration of a therapeutically-effective amount of thalidomide alone or in combination with other dermatological agents.
PI US 5654312 19970805 <--
SUMM . . . bites or may be idiopathic in nature. Results of skin biopsies for this condition are indicative of chronic dermatitis or **lichen** simplex chronicums. Diagnosis is made on the basis of clinical criteria. Mattos (Bol. Div. Nac. Lepra., 32:71) in 1973 was.
.
SUMM . . . a rare and severe illness of unknown etiology often afflicting young males. It is characterized by progressive ulceration of the **mouth** and genitalia, uveitis, and retinal vasculitis. There also may be atrophy of the gastrointestinal tract and pulmonary or myocardial
fibrosis.. . . treatment time of up to 65 months. Concomitant treatment in this patient group included 10 patients on prednisone, 3 on
azathioprine and 1 patient on cyclosporin. Mucosal lesions healed in all patients. Moulin et al. (Ann. Dermatol Venereol, 110:611, 1983) used. . . been used to treat recurrent erythema multiforme, a flu like syndrome in which blisters appear on mucous membranes of the **mouth** followed by lesions on the hands and feet. Corticosteroids are used to treat severe forms of the condition, however, the. . .
SUMM . . . as acute, chronic and physical urticarias, for example solar, cholinergic, pressure and cold urticarias. Atopic dermatitis; Mast Cell Disease, Bullous **Pemphigoid**; **Pemphigus** Vulgaris;

necrotizing vasculitis; lupus erythematosus (discold and systemic); dermatitis herpetiformis.

SUMM (f) Papulosquamous Dermatoses: such as Psoriasis, Pityriasis rosea, tinea versicolor, **lichen** planus.

SUMM . . . systemically administered corticosteroids are employed as therapeutics include psoriasis, erythema nodosum leprosum, discold lupus erythematosus, urticaria, different types of pruritis, **pemphigus** and keloids. Systemic administration of corticosteroids, however, is less than ideal therapy with the potential for any of the following. . .

L9 ANSWER 5 OF 18 USPATFULL

AB A method for the topical or systemic treatment of disorders mediated by proteases which result in skin or mucosal lesions, and in particular, **pemphigus**, cicatricial **pemphigoid**, bullous **pemphigoid**, **lichen** planus, and canker sores, is disclosed wherein the host is treated with an effective amount of N-acetyl ysteine or a derivative thereof, or its pharmaceutically acceptable salt, optionally in a pharmaceutically acceptable diluent or carrier for systemic or topical delivery.

PI US 5637616 19970610 <--

AB . . . the topical or systemic treatment of disorders mediated by proteases which result in skin or mucosal lesions, and in particular, **pemphigus**, cicatricial **pemphigoid**, bullous **pemphigoid**, **lichen** planus, and canker sores, is disclosed wherein the host is treated with an effective amount of N-acetyl ysteine or a. . .

SUMM . . . the skin and mucosal membranes which have been found to be mediated by proteases. Examples of protease mediated disorders include **lichen** planus, canker sores (aphthous ulcers), and a number of bullous diseases, including but not limited to **pemphigus**, bullous **pemphigoid** and cicatricial **pemphigoid**.

SUMM **Lichen** Planus

SUMM **Lichen** planus is a relatively common disease that results in cutaneous lesions and often oral lesions. Its prevalence averages between 0.5. . .

SUMM Although squamous cell carcinoma can arise in lesions of chronic oral **lichen** planus, **lichen** planus is often self-limiting and requires treatment only if it is symptomatic (Bleicher, P. A. in Manual of Clinical Problems in Dermatology, Olbricht, Bigby and Arndt, eds., 1992, Little, Brown & Co., Boston, pp. 85-89). In certain instances, however, **lichen** planus results in significant morbidity, and in the case of severe or chronic lesions involving mucosal surfaces, potentially debilitating pain.. . .

SUMM Systemic corticosteroid therapy may be of some benefit for the treatment of **lichen** planus (Arndt, K. in Fitzpatrick, Eisen, Wolff, Freedberg and Austen, Dermatology in General Medicine, 1987, Vol. 1, McGraw-Hill, Inc., New York, pp. 967-73). The most reliable method of treating ulcerative **lichen** planus symptoms is with intra-lesional steroid injections, which is often repeated at frequent intervals. Potent topical steroids such as beta-methasone. . . cyclosporine, and systemic antifungal agents, such as griseofulvin, have been reported to be somewhat effective in treating severely symptomatic oral **lichen** planus. No large, well designed studies, however, have proven the efficacy of these therapies. The use of potent topical steroids,. . .

SUMM . . . electrolyte imbalance or infection if serious bullous disease

is not adequately treated. Bullous diseases include, but are not limited to, **pemphigus**, bullous **pemphigoid**, and cicatricial **pemphigoid**. These three typical examples of bullous conditions are briefly described below.

SUMM **Pemphigus**

SUMM **Pemphigus** is an auto-immune disease of the skin which is manifested by the loss of intercellular adhesion between the keratinocytes (cells). . . in Manual of Clinical Problems in Dermatology, Olbricht, Bigby and Arndt eds., Little Brown & Co., Boston, 1992, pp. 56-60). **Pemphigus** can be further categorized by the specific site of the blisters in the various layers of the epidermis. **Pemphigus** vulgaris and **Pemphigus** vegetans exhibit blisters above the basal layer of the skin (i.e., the first layer of keratinocytes in the epidermis). In **Pemphigus** foliaceus and **Pemphigus** erythematosus, blister formation occurs just below the stratum corneum (i.e., higher in the epidermis).

SUMM **Pemphigus** vulgaris can affect all age groups. Lesions usually occur in the **mouth**, as well as on the chest, scalp, periumbilical, and intertriginous areas of the skin. Oral lesions frequently occur and may. . . the disease can involve the oropharynx and other mucosal surfaces, sometimes extending into the esophagus and cardia of the stomach. **Pemphigus** vulgaris is characterized by intra-epidermal blister formations due to acantholysis (i.e., loss of intercellular adhesions) in the superbasilar epidermis and. . .

SUMM **Pemphigus** vegetans is clinically manifested by vegetating legions and sometimes by pustules. The latter may represent super-infection at the edges of. . .

SUMM The blisters formed in **Pemphigus** foliaceus are superficial and easily ruptured. Primary symptoms often include crusting, scales, erosion, and excoriations.

SUMM **Pemphigus** erythematosus is similar to **Pemphigus** foliaceus histologically, and represents a localized form of **pemphigus**. Lesions of this type are characterized by a lupus-like butterfly rash as well as bullous and seborrheic dermatitis-like lesions. This type of **pemphigus** can be associated with other auto-immune diseases including rheumatoid arthritis, thymoma, myasthenia gravis and systemic lupus erythematosus.

SUMM Because of the severity of symptoms and the high morbidity and mortality associated with **pemphigus**, hospitalization is often necessary. Untreated or unresponsive **pemphigus** patients can develop sepsis, cachexia, and major fluid and electrolyte imbalances similar to those observed in burn patients.

SUMM Current treatment of **pemphigus** involves the use of corticosteroids, including high dosages of oral prednisone or prednisolone. Accordingly, these patients must be closely monitored for adrenocorticoid side effects. It has also been reported that immunosuppressive agents such as cyclophosphamide, **azathioprine**, methotrexate and cyclosporine-A, or a combination of immunosuppressive agents with high doses of prednisone may be useful in the symptomatic treatment of **pemphigus** (Lever, J. Am. Acad. Dermatol. 1979, Vol. 1, pp. 2-31). As with treatment with prednisone or prednisolone alone, patients undergoing immunosuppressive treatment must be closely monitored for adverse side effects. Treatment of **pemphigus** with gold compounds alone or in combination with prednisone has also been reported (Lever, J. Am. Acad. Dermatol. 1979, Vol.. . .

SUMM Bullous **Pemphigoid**

SUMM Bullous **pemphigoid** is the most common bullous disease of the skin. It is more prevalent in elderly patients than in younger patients.. . .

SUMM As with **pemphigus**, treatments for the various forms of bullous **pemphigoid** include systemic glucocorticosteroids. Often treatment will include an immuno-suppressive agent in addition to the steroids. Intra-lesional steroids may be beneficial. . .

SUMM Cicatricial **Pemphigoid**

SUMM Cicatricial **pemphigoid**, also called benign mucous membrane **pemphigoid** or ocular **pemphigoid**, is an uncommon chronic subepidermal bullous dermatosis which involves primarily the mucous membranes (Baden, L. A., Manual of Clinical Problems. . .

SUMM . . . Eisen, Wolff, Freedberg and Austen, Dermatology in General Medicine, 1987, Vol. 1, McGraw-Hill, Inc., New York, pp. 582-584). As with **pemphigus**, treatment of cicatricial **pemphigoid** often requires high doses of systemic corticosteroids and immunosuppressive agents. Because of the scarring associated with cicatricial **pemphigoid**, long term systemic steroids have been used in these patients despite the side effects. Cyclophosphamide, methotrexate, dapsone and **azathioprine** have been beneficial to some patients, while others have shown little improvement with these agents. Topical and intra-lesional steroids seem to be less effective in cicatricial **pemphigoid** than in oral **lichen** planus.

SUMM A common feature of **lichen** planus, **pemphigus**, bullous **pemphigoid**, cicatricial **pemphigoid** and **lichen** planus is the role of proteases in their pathogenesis. For example, in one study, cytotoxic proteases were identified in the blister fluid of **pemphigus** and **pemphigoid** patients (Grando, Glukhenky, Drannik, Kostromin and Chernyavsky, Int. J. Tissue React. 1989, Vol. 11, pp. 195-201). Similar observations have been. . . Singer, Sawka, Samowitz and Lazarus, J. Invest. Dermatol. 1980, Vol. 74, pp. 363-7). Inflammatory responses, such as those seen in **lichen** planus, result in the local production and/or elaboration of proteases and tissue injury at the disease site. (Barnhart, Quintana, Lenon,. . . Dermatol. 1989, Vol. 125, pp. 925-30; Forster, J. Dent. Res. 1972, Vol. 51, pp. 257-63). Finally, in the case of **pemphigus**, there is evidence that direct induction of proteinase activity by autoantibodies significantly contributes to the pathogenesis of the disease (Singer,. . .

SUMM . . . the mouse model. Based on this work, it appears that only certain proteinase inhibitors are effective in the treatment of **pemphigus**.

SUMM Aphthous ulcers are inflammatory lesions of unknown etiology that can effect any mucosal surface, but occur most often in the **mouth** (Cropley, T. G. in Manual of Clinical Problems in Dermatology, Olbricht, S. M., Bigby, M. E., Arndt, K. A., eds.. . .

SUMM . . . for the topical or systemic treatment of disorders mediated by proteases that cause skin or mucosal lesions, and in particular, **pemphigus**, cicatricial **pemphigoid**, bullous **pemphigoid**, **lichen** planus, and canker sores (aphthous ulcers), is disclosed wherein the host is treated with an effective amount of N-acetylcysteine ("NAC"). . .

DETD . . . (Morrison, Burnett and Stockley, Biol. Chem. Hoppe Seyler 1986, Vol. 367, pp. 177-82). Given the complexity of disorders such as **pemphigus**, cicatricial **pemphigoid**, bullous

pemphigoid, lichen planus, and canker sores, one could not predict from this report whether NAC would be an effective treatment in vivo. . .

DETD III. Methods for the Evaluation of Effectiveness of NAC in the Treatment of **Pemphigus** in Model Systems

DETD The effectiveness of N-acetylcysteine or its derivative or salt in the treatment of any of the forms of **pemphigus** described above can be evaluated by one or more of the following methods: (a) in an established organ culture model where the degree of acantholysis can be measured, after introduction of exogenous **pemphigus** antibody; (b) in a neonatal mouse model where disease can be induced, and evidence of clearing can be monitored; and or (c) in humans with **pemphigus**.

DETD 1. Experimental procedure for purification of **pemphigus** antibodies from human donors

DETD The **pemphigus** antibodies to be used in the analysis are purified and prepared in the following manner (Anhalt, Till, Diaz, Labib, Patel. . . Immunol. 1986, Vol. 137, pp. 2835-40). Serum is obtained from human patients with the clinical, histologic and immunologic features of **pemphigus**. The IgG fractions of the sera are purified by 40% ammonium sulfate precipitation, followed by ion exchange chromatography. IgG fractions. . . of the IgG, as known to those skilled in the art. The fractions are concentrated and sterilized via filtration. The **pemphigus** anti-body titer in the serum is then measured.

DETD 2. Organ Culture Model for **Pemphigus**

DETD . . . Dermatol. 1979, Vol. 1, pp. 2-31). Normal human skin is maintained in organ cultures to which sera of patients with **pemphigus** is added. Direct IF staining of the explants with fluorescein-labeled goat anti-human IgG shows that, after incubation, binding of the **pemphigus** IgG has occurred in the intercellular cement substance of the epidermis. Suprabasal acantholysis is observed which progresses to extensive acantholysis. Complement is not required for the in vitro production of acantholysis since heating the **pemphigus** sera at 56.degree. C. for thirty minutes does not prevent acantholysis (Lever, J. Am. Acad. Dermatol. 1979, Vol. 1, pp.. . .

DETD The ability of NAC or its derivative or salt to lessen or eliminate acantholysis in vitro caused by exposure to **pemphigus**-IgG the following experiment can be evaluated as follows. Normal human skin is cultured according to the method described by Naito,. . . atmosphere containing CO.sub.2 in air for 24, 48 and 72 hours. The culture medium should contain approximately 7 mg/mL of **pemphigus** IgG with or without the NAC or its derivatives or salts. After each culture period, the skin explants are examined. . . to 20 mg/mL. The skin can be preincubated (1-24 hours) with NAC, its derivative or salt prior to addition of **pemphigus** lgG. Acantholysis is evaluated on a scale of (-), (+), (++), or (+++), where (-) is no acantholysis, (+) is. . .

DETD 3. Neonatal Mouse Model for **Pemphigus**

DETD The ability of NAC or its derivative or salt to reduce the symptoms of **pemphigus** in vivo can be evaluated in a neonatal mice model (Anhalt, Labib, Voorhees, Beals and Diaz, N. Engl. J. Med.. . . pp. 41-46). Skin and serum samples are obtained from animals receiving injections of either normal human IgG (control) or human

pemphigus IgG. Skin samples from the flank region, where lesions most often occur are processed for direct immuno-fluorescence. Human **pemphigus** antibodies are also monitored in the animals' serum, to confirm transfer of the **pemphigus** antibodies. One group of mice is treated with topical administration of the test compound and monitored for disease improvement by. . .

DETD Specifically, within 30 minutes of **pemphigus** lgG injection, the neonatal mice receive injections of NAC, its salt, or its derivative prepared in PBS. The administered dosages. . . to be injected are sterilized by filtration through an 0.45 .mu.m millipore filter.

Effects of inhibitors on epidermal acantholysis by **pemphigus** IgG in neonatal mice are evaluated visually (positive if the presence of Nikolsky sign is observed; i.e., apparently normal epidermis. . . any part of the skin surface) as well as histologically (acantholytic changes are examined at five sites) 24 hours after **pemphigus** IgG is injected. To carry out biochemical analysis 24 hours after **pemphigus** IgG injection the mice are sacrificed and the whole skin of each animal removed. At least five different sites from. . .

DETD . . . neonatal mouse epidermis is determined. Skin samples are removed as described above at 3 and 24 hours after injection of **pemphigus** IgG with preinjection of the test compound. The skin is isolated by heating the skin at 56.degree. C. for 30. . .

DETD The effectiveness of treatment of patients with oral lesions resulting from **lichen** planus, bullous **pemphigoid**, cicatricial **pemphigoid**, **pemphigus** or canker sores (aphthous uclers) with NAC or its derivatives or salts thereof can be evaluated as described generally for treatment of **lichen** planus by Eisen, Ellis, Duell, Griffiths and Voorhees, in N. Engl. J. Med. 1990, Vol. 323, pp. 290-4. For example, patients with symptomatic oral **lichen** planus are given either placebo or a topical N-acetylcysteine solution, gel, or ointment containing 1 to 50% NAC or other. . .

CLM What is claimed is:

. . . of disorders mediated by proteases in mammals that result in skin or mucosal lesions selected from the group consisting of **lichen** planus, canker sores (aphthous ulcers), and bullous diseases, comprising: topically applying to the skin or mucosal lesion an effective amount. . .

. . . of disorders mediated by proteases in mammals that result in skin or mucosal lesions selected from the group consisting of **lichen** planus, canker sores (aphthous ulcers), and bullous diseases, comprising: systemically administering to a mammal in need thereof an effective amount. . .

. . . of disorders mediated by proteases in mammals that result in skin or mucosal lesions selected from the group consisting of **lichen** planus, canker sores (aphthous ulcers), and bullous diseases, comprising: topically applying to the skin or mucosal lesion an effective amount. . .

. . . of disorders mediated by proteases in mammals that result in skin or mucosal lesions selected from the group consisting of **lichen** planus, canker sores (aphthous ulcers), and bullous diseases, comprising: systemically administering an effective amount of a derivative of N-acetylcysteine of. . .

25. The method of claim 1 wherein the disease is **pemphigus**.

26. The method of claim 1 wherein the disease is bullous **pemphigoid.**

27. The method of claim 1 wherein the disease is cicatricial **pemphigoid.**

28. The method of claim 1 wherein the disease is **lichen** planus.

30. The method of claim 2 wherein the disease is **pemphigus.**

31. The method of claim 2 wherein the disease is bullous **pemphigoid.**

32. The method of claim 2 wherein the disease is cicatricial **pemphigoid.**

33. The method of claim 2 wherein the disease is **lichen** planus.

35. The method of claim 3 wherein the disease is **pemphigus.**

36. The method of claim 3 wherein the disease is bullous **pemphigoid.**

37. The method of claim 3 wherein the disease is cicatricial **pemphigoid.**

38. The method of claim 3 wherein the disease is **lichen** planus.

40. The method of claim 4 wherein the disease is **pemphigus.**

41. The method of claim 4 wherein the disease is bullous **pemphigoid.**

42. The method of claim 4 wherein the disease is cicatricial **pemphigoid.**

43. The method of claim 4 wherein the disease is **lichen** planus.

L9 ANSWER 6 OF 18 USPATFULL

AB A method for the treatment of a cutaneous, ocular, or mucosal pathological condition which is associated with immune response in a human or other mammal, that includes topical application of an effective amount of spiperone or a spiperone derivative or its pharmaceutically acceptable salt, in a pharmaceutically-acceptable diluent or carrier for topical application.

PI US 5244902 19930914 <--

SUMM . . . Sjogren's Syndrome, alopecia areata, allergic responses due to arthropod bite reactions, Crohn's disease, aphthous ulcer, iritis, conjunctivitis, keratoconjunctivitis, ulcerative colitis, **lichen** planus, asthma, allergic asthma, cutaneous lupus erythematosus, scleroderma, vaginitis, proctitis, and drug eruptions. These conditions may result in any one. . .

SUMM . . . agents with partial utility for treating some of the above

conditions include psoralen plus ultraviolet A (PUVA), cyclosporin A, or
azathioprine, but the risk-to-benefit ratios for these agents is unfavorable for most of the conditions described above.
DETD . . . can be treated by topical application of spiperone or spiperone
derivatives include contact dermatitis, atopic dermatitis, eczematous dermatitis, drug eruptions, **lichen** planus, psoriasis, alopecia areata, Sjogren's Syndrome, including keratoconjunctivitis sicca secondary to Sjogren's Syndrome, cutaneous lupus erythematosus, scleroderma, allergic reactions secondary. . .
CLM What is claimed is:
. . . oral or mucosal, an the the spiperone or spiperone derivative is administered in a solution that is swished in the **mouth** and spit out.

L9 ANSWER 7 OF 18 USPATFULL
AB A pharmaceutical composition and a method for its use in the treatment of severe chronic inflammatory diseases, such as demyelinating disease, uveitis and graft-versus-host disease are provided. The composition comprises tumor necrosis factor as an active ingredient and at least one
pharmaceutically acceptable carrier, diluent or excipient.
PI US 5190750 19930302 <--
SUMM . . . GVHD and generalized GVHD according to the clinical findings. The main symptom of localized GVHD are lesions which include drying, **lichen** planus-like change, pigmentation, depigmentation and erythema accompanied with detachment. It sometimes accompanies with liver disorders. The syndrome of generalized GVHD consists of affections
of the mucous membrane of the salivary gland, the **mouth** and the esophagus, the iachrymals, the lung, the bronchus, muscle and the joint. These symptoms lead to a reversion of. . .
SUMM As therapeutic methods for GVHD, general administration of immunosuppressive agents, such as methotrexate, steroids, **azathioprine** and cyclosporine A has been conventionally utilized. However, they have problems with side effects which have yet to be solved.

L9 ANSWER 8 OF 18 MEDLINE
AB Systemic corticosteroids are of value in severe **lichen** planus which interferes with the patient's life or is ulcerative or where there is nail destruction. **Azathioprine** has been shown to be effective steroid sparing treatment for generalized **lichen** planus. We report two patients with severe **lichen** planus who responded to **azathioprine** alone and suggest it may be an alternative therapy, especially when there are risk factors against corticosteroid use. **Lichen** planus accounts for approximately 1% of new presentations to a dermatology unit. It can affect all body areas and markedly interfere
with a patient's life. Mucous membrane lesions are common (30-70%) but ulcerative lesions in the **mouth** are uncommon. **Lichen** planus seems to be immunologically mediated with evidence favouring a lymphocytotoxic process described in the literature. Treatment is mainly symptomatic and can be difficult. Systemic corticosteroids are of value in
treating severe cases where the disease is interfering with a patient's life or when ulcerative mucous membrane lesions have occurred or if there is severe nail destruction. Relapse can occur on cessation of steroids.

Azathioprine has been shown to be effective steroid sparing therapy for generalized **lichen** planus. However, the use of **azathioprine** alone has not been described. We report two cases of generalized, erosive **lichen** planus that responded well to **azathioprine** alone.

TI Erosive and generalized **lichen** planus responsive to **azathioprine**.

SO CLINICAL AND EXPERIMENTAL DERMATOLOGY, **(1996 Jan)** 21 (1) 56-7. Journal code: DDU; 7606847. ISSN: 0307-6938.

AB Systemic corticosteroids are of value in severe **lichen** planus which interferes with the patient's life or is ulcerative or where there is nail destruction. **Azathioprine** has been shown to be effective steroid sparing treatment for generalized **lichen** planus. We report two patients with severe **lichen** planus who responded to **azathioprine** alone and suggest it may be an alternative therapy, especially when there are risk factors against corticosteroid use. **Lichen** planus accounts for approximately 1% of new presentations to a dermatology unit. It can affect all body areas and markedly interfere with a patient's life. Mucous membrane lesions are common (30-70%) but ulcerative lesions in the **mouth** are uncommon. **Lichen** planus seems to be immunologically mediated with evidence favouring a lymphocytotoxic process described in the literature. Treatment is mainly symptomatic. . . ulcerative mucous membrane lesions have occurred or if there is severe nail destruction. Relapse can occur on cessation of steroids. **Azathioprine** has been shown to be effective steroid sparing therapy for generalized **lichen** planus. However, the use of **azathioprine** alone has not been described. We report two cases of generalized, erosive **lichen** planus that responded well to **azathioprine** alone.

CT Check Tags: Case Report; Female; Human
Aged
***Azathioprine: TU, therapeutic use**
*Immunosuppressive Agents: TU, therapeutic use
***Lichen Planus: DT, drug therapy**
Lichen Planus: PA, pathology
Middle Age
Treatment Outcome

RN **446-86-6 (Azathioprine)**

L9 ANSWER 9 OF 18 MEDLINE

AB **Pemphigus** vulgaris during pregnancy is exceedingly rare; only 15 cases with immunopathologic confirmation have been reported. In the four cases associated with fetal mortality the mother's disease was active and required high doses of corticosteroids and adjuvant therapy with **azathioprine** or dapsone for control. A pregnant woman with limited disease is described. At the time of delivery her **pemphigus** vulgaris antibody titer was 1:640. A full-term, healthy male infant was completely free of skin lesions after a spontaneous vaginal delivery.

TI **Pemphigus** vulgaris and pregnancy: risk factors and recommendations.

SO JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY, **(1993 May)** 28 (5 Pt 2) 877-9. Journal code: HVG; 7907132. ISSN: 0190-9622.

AB **Pemphigus** vulgaris during pregnancy is exceedingly rare; only 15 cases with immunopathologic confirmation have been reported. In the four cases associated with fetal mortality the mother's disease was active and required high doses of corticosteroids and adjuvant therapy with **azathioprine** or dapsone for control. A pregnant woman with limited

disease is described. At the time of delivery her **pemphigus** vulgaris antibody titer was 1:640. A full-term, healthy male infant was completely free of skin lesions after a spontaneous vaginal. . .

CT Check Tags: Case Report; Female; Human
Adult
Mouth Diseases: PA, pathology
***Pemphigus**
Pemphigus: PA, pathology
Pregnancy
*Pregnancy Complications
Pregnancy Complications: PA, pathology
Risk Factors
Vaginal Diseases: PA, pathology

L9 ANSWER 10 OF 18 MEDLINE

AB This case of CP is of interest because of its "not-so-benign" course in this patient, its unusual immunofluorescence patterns, and the need for a complex therapeutic regimen to achieve control. This patient had severe ocular; laryngeal, and oropharyngeal involvement leading to visual problems, hoarseness, and marked weight loss and dehydration. He also had anemia thought to be partially related to dapsone use. We believe the side effects of dapsone, combined with fluid retention due to prednisone therapy, contributed to cardiac failure. The diagnosis of CP is usually established by correlation of clinical findings with immunofluorescence studies. However, indirect immunofluorescence may show strong intercellular antibody binding in the epidermis (ie, **pemphigus**-like antibodies). Treatment alternatives for patients with CP who have adverse reactions to, or no significant benefit from, conventional agents such as dapsone or prednisone may include immunosuppressive agents such as **azathioprine** or cyclophosphamide. As this case demonstrates, care of patients having CP involves a cooperative effort from a number of different specialties, including dermatology, primary care, ophthalmology, and otolaryngology.

TI Cicatricial **pemphigoid**.

SO SOUTHERN MEDICAL JOURNAL, **(1993 Apr)** 86 (4) 461-4.
Journal code: UVH; 0404522. ISSN: 0038-4348.

AB . . . correlation of clinical findings with immunofluorescence studies.
However, indirect immunofluorescence may show strong intercellular antibody binding in the epidermis (ie, **pemphigus**-like antibodies). Treatment alternatives for patients with CP who have adverse reactions to, or no significant benefit from, conventional agents such as dapsone or prednisone may include immunosuppressive agents such as **azathioprine** or cyclophosphamide. As this case demonstrates, care of patients having CP involves a cooperative effort from a number of different. . .

CT Check Tags: Case Report; Human; Male
Aged
***Azathioprine: TU, therapeutic use**
Dapsone: TU, therapeutic use
Fluorescent Antibody Technique
Mouth Mucosa: PA, pathology
***Pemphigoid, Benign Mucous Membrane: DT, drug therapy**
Pemphigoid, Benign Mucous Membrane: PA, pathology
Prednisone: TU, therapeutic use

RN **446-86-6 (Azathioprine)**; 53-03-2 (Prednisone); 80-08-0 (Dapsone)

L9 ANSWER 11 OF 18 MEDLINE

AB This article reviews our experience during a 20-year period with patients with oral lesions of **pemphigus** vulgaris. Of the 30 patients, 20 were women and 10 were men, with an age range of 24 to 68 years. The soft palate was involved in 80% of cases at initial presentation. Direct immunofluorescence studies were positive for IgG in the intercellular region in all cases where lesional tissue was histologically studied. Systemic steroid therapy alone controlled the disease in 24 patients, one patient was given no treatment, and the remaining five required additional treatment with either **azathioprine**, cyclophosphamide, or gold. Steroid therapy was continued in the long-term at a reduced dose, but side effects such as diabetes mellitus, hypertension, and duodenal ulcers were observed. Long-term steroid therapy is therefore the treatment of choice for the oral lesions of **pemphigus** vulgaris, but in some cases alternative treatment options may be required.

TI Oral presentation of **pemphigus** vulgaris and its response to systemic steroid therapy.

SO ORAL SURGERY, ORAL MEDICINE, AND ORAL PATHOLOGY, **(1992 Jul)** 74 (1) 54-7.
Journal code: OJU; 0376406. ISSN: 0030-4220.

AB This article reviews our experience during a 20-year period with patients with oral lesions of **pemphigus** vulgaris. Of the 30 patients, 20 were women and 10 were men, with an age range of 24 to 68. . . . the disease in 24 patients, one patient was given no treatment, and the remaining five required additional treatment with either **azathioprine**, cyclophosphamide, or gold. Steroid therapy was continued in the long-term at a reduced dose, but side effects such as diabetes. . . . hypertension, and duodenal ulcers were observed. Long-term steroid therapy is therefore the treatment of choice for the oral lesions of **pemphigus** vulgaris, but in some cases alternative treatment options may be required.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
Azathioprine: TU, therapeutic use
Cyclophosphamide: TU, therapeutic use
Middle Age
***Mouth Diseases: DT, drug therapy**
***Pemphigus: DT, drug therapy**
Prednisolone: TU, therapeutic use

RN **446-86-6 (Azathioprine)**; 50-18-0 (Cyclophosphamide); 50-24-8 (Prednisolone)

L9 ANSWER 12 OF 18 MEDLINE

AB The initial oral findings and treatment in 50 cases of mucous membrane **pemphigoid** are presented. Histologic and immunologic studies were undertaken in each case to confirm the clinical diagnosis. The treatments prescribed are summarized and illustrate that topical steroids are effective, but in some cases systemic steroid therapy with or without other immunologically active drugs is required. A significant number of patients had extraoral manifestations of the disorder.

TI Mucous membrane **pemphigoid**. Treatment experience at two institutions.

SO ORAL SURGERY, ORAL MEDICINE, AND ORAL PATHOLOGY, **(1992 Jul)** 74 (1) 50-3.
Journal code: OJU; 0376406. ISSN: 0030-4220.

AB The initial oral findings and treatment in 50 cases of mucous membrane **pemphigoid** are presented. Histologic and immunologic studies were

undertaken in each case to confirm the clinical diagnosis. The treatments prescribed are. . .

CT Check Tags: Female; Human; Male
Adolescence
Adult
Aged
Azathioprine: TU, therapeutic use
Cyclophosphamide: TU, therapeutic use
Dapsone: TU, therapeutic use
Gingival Diseases: DT, drug therapy
Glucocorticoids, Topical: TU, therapeutic use
Middle Age
Mouth Diseases: DT, drug therapy
Mouth Mucosa
***Pemphigoid, Benign Mucous Membrane: DT, drug therapy**
Prednisolone: TU, therapeutic use

RN **446-86-6 (Azathioprine)**; 50-18-0 (Cyclophosphamide); 50-24-8 (Prednisolone); 80-08-0 (Dapsone)

L9 ANSWER 13 OF 18 MEDLINE

AB The findings in this prospective study of 214 patients with oral **lichen** planus were similar to those found in our 1985 evaluation of 570 patients with oral **lichen** planus. These two groups of patients with oral **lichen** planus patients constitute the largest series from one clinic. Oral **lichen** planus was found mainly in women and most commonly on the buccal mucosa. Spontaneous remissions were infrequent (6.5%), as were malignant transformations (2.3%) in a mean follow-up of 7.5 years. The erosive form of oral **lichen** planus was most common and was almost always associated with pain. Reproducibly successful management of this T-lymphocyte disease was obtained by selective use of systemic and/or topical corticosteroids. Oral **lichen** planus was not associated with any evident systemic disease, drug, smoking, or genetic predisposition. Although statistically Candida albicans does not appear to occur disproportionately in large samples of patients with oral **lichen** planus, in some of the Candida-positive patients, antifungal medications appeared to be useful.

TI A prospective study of findings and management in 214 patients with oral **lichen** planus.

SO ORAL SURGERY, ORAL MEDICINE, AND ORAL PATHOLOGY, **(1991 Dec)** 72 (6) 665-70.
Journal code: OJU; 0376406. ISSN: 0030-4220.

AB The findings in this prospective study of 214 patients with oral **lichen** planus were similar to those found in our 1985 evaluation of 570 patients with oral **lichen** planus. These two groups of patients with oral **lichen** planus patients constitute the largest series from one clinic. Oral **lichen** planus was found mainly in women and most commonly on the buccal mucosa. Spontaneous remissions were infrequent (6.5%), as were malignant transformations (2.3%) in a mean follow-up of 7.5 years. The erosive form of oral **lichen** planus was most common and was almost always associated with pain. Reproducibly successful management of this T-lymphocyte disease was obtained by selective use of systemic and/or topical corticosteroids. Oral **lichen** planus was not associated with any evident systemic disease, drug, smoking, or genetic predisposition. Although statistically Candida albicans does not appear to occur disproportionately in large samples of patients with oral **lichen** planus, in some of the Candida-positive patients, antifungal medications appeared to be useful.

CT Check Tags: Female; Human; Male
Administration, Oral
Adult

Aged
Aged, 80 and over
Azathioprine: TU, therapeutic use
Carboxymethylcellulose: TU, therapeutic use
Fluocinonide: TU, therapeutic use
Follow-Up Studies
***Lichen Planus: DT, drug therapy**
***Lichen Planus: PA, pathology**
Middle Age
Mouth Diseases: DT, drug therapy
***Mouth Diseases: PA, pathology**
Prednisone: AD, administration & dosage
Prospective Studies
Treatment Outcome

RN 356-12-7 (Fluocinonide); **446-86-6 (Azathioprine)**; 53-03-2 (Prednisone); 81209-86-1 (Orabase); 9004-32-4 (Carboxymethylcellulose)

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574/261

=> s purine

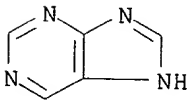
L3 33025 PURINE

=> s purine/cn

L4 1 PURINE/CN

=> d l4

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 120-73-0 REGISTRY
CN 1H-Purine (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Purine (6CI, 8CI)**
OTHER NAMES:
CN .beta.-Purine
CN 3,5,7-Triazaindole
CN 6H-Imidazo[4,5-d]pyrimidine
CN 7H-Purine
CN 9H-Purine
CN Isopurine
FS 3D CONCORD
DR 273-25-6, 273-26-7, 111055-93-7
MF C5 H4 N4
CI COM, RPS
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DETHERM*, EMBASE, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, TULSA, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



3655 REFERENCES IN FILE CA (1967 TO DATE)
2141 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3658 REFERENCES IN FILE CAPLUS (1967 TO DATE)
74 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

514/262

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 s azathioprine

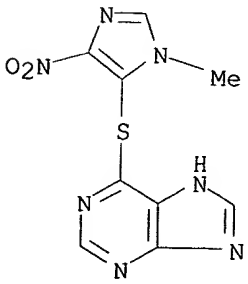
L1            9 AZATHIOPRINE

=> s azathioprine/cn

L2            1 AZATHIOPRINE/CN

=> d
```

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 446-86-6 REGISTRY
CN 1H-Purine, 6-[(1-methyl-4-nitro-1H-imidazol-5-yl)thio]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Purine, 6-[(1-methyl-4-nitroimidazol-5-yl)thio]- (6CI, 8CI)
OTHER NAMES:
CN 6-(1-Methyl-4-nitroimidazol-5-yl)thiopurine
CN 6-(1-Methyl-4-nitromidazol-5-ylthio)purine
CN Azathioprin
CN **Azathioprine**
CN Azothioprine
CN BW 57-322
CN Imuran
CN Imurek
CN Imurel
CN Muran
CN NSC 39084
FS 3D CONCORD
DR 11120-16-4, 6165-04-4, 33609-91-5
MF C9 H7 N7 O2 S
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PROMT, RTECS*, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



1696 REFERENCES IN FILE CA (1967 TO DATE)
18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1697 REFERENCES IN FILE CAPLUS (1967 TO DATE)